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10/635,241	08/05/2003	Zhen Zhang	58369 (71699)	6657

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EXAMINER
DEJONG, ERIC S

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)
Office Action Summary	10/635,241	ZHANG ET AL.
	Examiner	Art Unit	
	ERIC S. DEJONG	1631	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
 Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on <u>11 March 2008</u>.

2a)☒ This action is **FINAL**.   2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) <u>See Continuation Sheet</u> is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) <u>See Continuation Sheet</u> is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-224.

Continuation of Disposition of Claims: Claims rejected are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-224.

DETAILED OFFICE ACTION

Applicants response filed 03/11/2008 is acknowledged.

Claims 1-111, 119, 121, 122, 125, 126, 128-130, 135, 136, 140, 146, 154-160, 162-164, 169, 170, 174, 179, 191, 193-195, 198, 199, 201-203, 206-209, 213, and 218 are canceled. Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-224 are pending and currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 101

The rejection of claims 182-190, 192, 196, 197, 200, 204-207, 210-212, 214-217,

219, and 220 under 35 USC § 101 because the claimed invention is directed to non-

statutory subject matter is withdrawn in view of amendments made to the instant claims.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, and 181 are

rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory

subject matter. The grounds of this rejection have changed and are necessitated by

amendments made to the instant claims.

Regarding data structures representing descriptive material and computer

programs, MPEP § 2106.01(I) states:

"Data structures not claimed as embodied in computer-readable media are descriptive material per se and are not statutory because they are not capable of causing functional change in the computer. See, e.g., Warmerdam, 33 F.3d at 1361, 31 USPQ2d at 1760 (claim to a data structure per se held nonstatutory). Such claimed data structures do not define any structural and functional interrelationships between the data structure and other claimed aspects of the invention which permit the data structure's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a data structure defines structural and functional interrelationships between the data structure and the computer software and hardware components which permit the data structure's functionality to be realized, and is thus statutory.
Similarly, computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical "things." They are neither computer components nor statutory processes, as they are not "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory. See Lowry, 32 F.3d at 1583-84, 32 USPQ2d at 1035. Accordingly, it is important to distinguish claims that define descriptive material per se from claims that define statutory inventions."

Claim 149 now recites the limitation "A computer readable program product embodied in a written electronic, magnetic or optical media comprising" in lines 1 and 2 of said claim. The instant claims encompass on a written computer listing that does not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. Rather, the written computer listing as instantly claimed encompasses nonfunctional descriptive material, *per se*, and is therefore not statutory subject matter. The instant claims further encompass embodiments wherein the electronic and magnetic media encompass signal and carrier wave embodiments that are also not statutory subject matter. See *In re Nuitjen* (2007). Claims 150-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, and 181, which depend from claim 149, are also included under this rejection.

Response to Arguments

Applicant's arguments filed 03/11/2008 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC 101 as being directed to non-statutory subject matter, applicants argue that the rejection has been rendered moot in view of amendments made to the instant claims.

In response, it is first noted that the amendments to instant claim 149 are not sufficient to overcome the rejection. It is reiterated from the instant rejection that the written computer listing as instantly claimed encompasses nonfunctional descriptive

material, *per se*, and is therefore not statutory subject matter. Further, the instant claims

further encompass embodiments wherein the electronic and magnetic media

encompass signal and carrier wave embodiments that are also not statutory subject

matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of

the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g)

prior art under 35 U.S.C. 103(a).

Claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and

221-224 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The*

Lancet, 359:572-577 (February 16, 2002)) in view of Golub (*Science,* 286:531-537 (Oct.

15, 1999)).

Petricoin discloses analyzing two biological state classes – "unaffected" and

"affected" wherein the affected group is known to have cancer. Petricoin discloses

analyzing two independent sets of samples. Specifically, one "sample" is composed of

50 control samples for preliminary analysis, other 17 control samples, and samples from

cancer patients for preliminary analysis (*see* p. 572-573, Methods and *Study*

Population; table 1; fig. 1, p. 575, and p. 576). Thus, the analysis of the original test data

is analysis of "the first set" of samples. A second "sample set" is composed of 50 control

samples for the masked analysis, other unaffected samples, and benign disease control

samples (p. 573-573; fig. 1, p. 575, and p. 576). Petricoin teaches that results from the

test (masked data) may be added to the model/dataset to improve prediction (p. 576,

right col., third full paragraph). Therefore, Petricoin discloses that both "samples" were

collected and separately statistically analyzed to classify samples into different

biological states (*e.g.*, cancer and unaffected states) (fig. 1, p. 575, table 2, p. 576, left

col.) AND also discloses an "intersection" subset (the totality of the data used for

classification after "improvement"). Also, the results obtained from two independent

samples (preliminary and masked) were "intersected" wherein data elements (key

values for classifying samples, *e.g.*, M/Z) in the intersection subset is a member of both

subsets (preliminary and masked samples) (p. 576). Petricoin teaches selecting a first

subset of data elements from the first data (key M/Z values) (fig. 1 and p. 575 and 576).

Petricoin further discloses a preanalytical variable, *e.g.*, medical status, a clinical

characteristic, medical condition (*e.g.*, premenopausal, menopause, age, benign

diseases, *etc.*) and age distribution (*see* table 1, p. 573, p. 576). Petricoin discloses

samples collected at different locations (*e.g.,* 100 control samples were provided from

NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the

Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573). Petricoin teaches

using different assays for training and validation (masked) data wherein "masking" adds

an additional step to the method (p. 575, left col.). Petricoin discloses reshuffling

(resampling) of the two highest rated sets to form new subset candidates (p. 575).

Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation

data set (masked serum samples, p. 575 and p. 577). Petricoin discloses a biological

state is a characteristic of presence of a disease (cancer) and a biomarker is a

diagnostic of a disease (CA125). Petricoin teaches that values of data elements

represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z

values determined by MS, p. 573; see also peaks on fig. 2). Expression of a law-

molecular-weight protein (a cancer antigen CA125) is measured by coupling serum

samples with a C16 hydrophobic interaction protein chip array (an immobilized capture

affinity array) and the amount of the protein is measured by SELDI-TOF mass

spectrometry (p. 573, right col.). The sample of Petricoin is serum and data collected

from serum relate to the cellular localization of components in a sample (*e.g.,*

components located in a soluble cell fraction or "attached" to suspended cell

membranes) (p. 573, left col.). Petricoin teaches using different assays for training and

validation (masked) data wherein "masking" adds an additional step to the method (p.

575, left col.). Petricoin also discloses "pattern-recognition" (p. 576, right col., third full

paragraph, line 10). Petricoin discloses a "classification" as a pattern recognition process (fig. 1; p. 575, left col.).

Petricoin does not expressly teach selecting a second subset and displaying the intersection subset.

Golub discloses a method for classifying cancer by using gene expression monitoring (p. 531). Golub discloses using two classes (ALL and AML acute leukemia) and two samples comprising both classes (38 initial leukemia samples and independently collected 34 leukemia samples) (p. 532, 534). Golub discloses selecting "predictors" from the first sample (38 samples) and testing the predictors on an independent 34 leukemia samples (p. 532). Golub further discloses prediction strengths for both the initial (cross-validation) sample and an independent sample and selection of data elements with high prediction strength for both samples (selecting a first and a second subset) (p. 543 and fig. 3). Golub also discloses comparing two samples wherein the structure (data elements – gene predictors) in the initial sample is also seen in the independent sample (i.e., samples are intersected) (p. 534, middle col. and fig. 4). Golub discloses displaying the intersection (fig. 3). Golub discloses that different types of samples, bone marrow and blood, were collected by different protocols (e.g., samples from SJCRH were processed with a very different protocol) (p. 536-537, paragraph 23). Also, collection of bone marrow and blood requires different protocols. Golub discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to select both a first and a second subset of data elements and display the intersection, as taught by Golub, where the motivation would have been to test a model/hypothesis and to compare results from a model and a test, as taught by Golub, p. 534.

Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct. 15, 1999)), as applied to claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and 221-224 above, and in further view of Barnhill (U.S. Patent 6,789,069).

Petricoin and Golub make obvious claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 148, and 221-224, as set forth above.

Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and processing experimental data and bioinformatics software for processing data (p. 573 and 575). Petricoin discloses a computer based chip system (the Protein Biology System 2 SELDI-TOF mass spectrometer such as Ciphergen Biosystems with a detector and a chip reader, p. 573). Petricoin also discloses that data were collected and were used later for analysis (*i.e.*, data are stored).

Petricoin and Golub do not disclose a supervised learning algorithm and specifically, a support vector machine analysis; protein binding partners in an

expression profiling assay; and a computer system and a computer readable medium for performing the method.

Barnhill discloses a method for classifying unknown samples using a learning machine, similar to that of Petricoin. Barnhill discloses different methods for data acquisition such as nucleic acid arrays and protein expression assays (*e.g.*, antibody chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col, 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (*see* for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a supervised learning algorithm and specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre-and post-processing data and maximize the

value of genomic and proteomic information, as taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 – col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Response to Arguments

Applicant's arguments filed 03/11/2008 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and in further view of Barnhill, applicants argue that Petricon does not teach the selection of subsets from the first and second data sets nor does Petricon teach or suggest the selection of an intersection subset from these subsets. Applicants further argue that Petricon nor any other cited documents (i.e. Golub and Barnhill) disclose or suggest the step of selecting an intersection subset of data elements as recited in claim 112, a third computer readable program providing

instructions for selection an intersection subset of data elements, as recited in claim
149, executing computer readable program code for selecting an intersection subset of
data elements as recited in claim 182.

In response to applicant's arguments against the references individually, one
cannot show nonobviousness by attacking references individually where the rejections
are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208
USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.
1986). It is reiterated from the instant rejection that Petricoin does not expressly teach
selecting a second subset and displaying the intersection subset. Golub is relied upon in
the instant rejection for disclosing the comparison of samples wherein the structure
(data elements – gene predictors) in the initial sample is also seen in the independent
sample (*i.e.*, samples are intersected) (p. 534, middle col. and fig. 4) and further
displaying the intersection (fig. 3). Applicants argument is essentially an assertion that
Golub fails to teach the deficiencies of Petricon and fails to point out the patentable
novelty of the instant claims over that of the state of the art disclosed by the cited
references. Therefore applicants argument is not persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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USPTO Customer Service Representative or access to the automated information

system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S DeJong/
Primary Examiner, Art Unit 1631